

## PATENT COOPERATION TREATY

PCT

## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

United States Patent and Trademark  
Office  
(Box PCT)  
Crystal Plaza 2  
Washington, DC 20231  
ÉTATS-UNIS D'AMÉRIQUE

in its capacity as elected Office

Date of mailing (day/month/year)

12 March 1999 (12.03.99)

International application No.

PCT/US98/15411

Applicant's or agent's file reference

234/231 PCT

International filing date (day/month/year)

24 July 1998 (24.07.98)

Priority date (day/month/year)

25 July 1997 (25.07.97)

Applicant

BRIGGS, Michael, R. et al

1. The designated Office is hereby notified of its election made:



in the demand filed with the International Preliminary Examining Authority on:

12 February 1999 (12.02.99)



in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was

was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

A. Karkachi

Telephone No.: (41-22) 338.83.38

## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

REC'D 21 MAY 1999

WIPO PCT

Applicant's or agent's file reference 234/231-PCT	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US98/15411	International filing date (day/month/year) 24 JULY 1998	Priority date (day/month/year) 25 JULY 1997
International Patent Classification (IPC) or national classification and IPC Please See Supplemental Sheet.		
Applicant LIGAND PHARMACEUTICALS INCORPORATED		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 2 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of report with regard to novelty, inventive step or industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 12 FEBRUARY 1999	Date of completion of this report 06 MAY 1999
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	Authorized officer IREM YUCEL
Facsimile No. (703) 305-3230	Telephone No. (703) 308-0196

JOYCE BRIDGERS  
PARALEGAL SPECIALIST  
CHEMICAL MATRIX

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US98/15411

## I. Basis of the report

1. This report has been drawn on the basis of *(Substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments):*

- ☒ the international application as originally filed.
- ☒ the description, pages 1-86 , as originally filed.  
pages NONE , filed with the demand.  
pages NONE , filed with the letter of \_\_\_\_\_.  
pages \_\_\_\_\_ , filed with the letter of \_\_\_\_\_.
- ☒ the claims, Nos. 1-25 , as originally filed.  
Nos. NONE , as amended under Article 19.  
Nos. NONE , filed with the demand.  
Nos. NONE , filed with the letter of \_\_\_\_\_.  
Nos. \_\_\_\_\_ , filed with the letter of \_\_\_\_\_.
- ☒ the drawings, sheets/fig 1-7 , as originally filed.  
sheets/fig NONE , filed with the demand.  
sheets/fig NONE , filed with the letter of \_\_\_\_\_.  
sheets/fig \_\_\_\_\_ , filed with the letter of \_\_\_\_\_.

2. The amendments have resulted in the cancellation of:

- ☒ the description, pages none .
- ☒ the claims, Nos. none .
- ☒ the drawings, sheets/fig none .

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the ~~Supplemental Box~~ Additional observations below (Rule 70.2(c)).

4. Additional observations, if necessary:

NONE

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.  
PCT/US98/15411**III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

The question whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been and will not be examined in respect of:

☐ the entire international application.

☒ claims Nos. 9-14

because:

☐ the said international application, or the said claim Nos. \_ relate to the following subject matter which does not require international preliminary examination (*specify*).

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. \_ are so unclear that no meaningful opinion could be formed (*specify*).

☐ the claims, or said claims Nos. \_ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 9-14.

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US98/15411

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement****1. STATEMENT**

Novelty (N)	Claims <u>1-8 and 15-25</u>	YES
	Claims <u>none</u>	NO
Inventive Step (IS)	Claims <u>1-8 and 15-25</u>	YES
	Claims <u>none</u>	NO
Industrial Applicability (IA)	Claims <u>1-8 and 15-25</u>	YES
	Claims <u>none</u>	NO

**2. CITATIONS AND EXPLANATIONS**

Claims 1-8 and 15-25 meet the criteria set out in PCT Article 33(2)-(4), because the prior art does not teach or fairly suggest the control regions of the human PPAR $\gamma$  gene. The prior art does not teach nor fairly suggest methods of screening for agents which modulate expression of the human PPAR $\gamma$  gene by using the control region of the human PPAR $\gamma$  gene in reporter gene constructs. Further the claimed invention recited by the instant claims has industrial applicability.

----- NEW CITATIONS -----  
NONE

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US98/15411

**Supplemental Box**

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

Sheet 10

**CLASSIFICATION:**

The International Patent Classification (IPC) and/or the National classification are as listed below:

IPC(6): C07H 21/02, 21/04; C12N 5/06, 5/08, 5/10; C12Q 1/02, 1/68; C12P 21/06 and US Cl.: 536/23.1, 23.5, 24.1; 435/6, 29, 69.1, 357, 365, 370

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US98/15411

**A. CLASSIFICATION OF SUBJECT MATTER**

IPC(6) : Please See Extra Sheet.

US CL : 536/23.1, 23.5, 24.1; 435/6, 29, 69.1, 357, 365, 370

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 536/23.1, 23.5, 24.1; 435/6, 29, 69.1, 357, 365, 370

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched  
NONE

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
Please See Extra Sheet.

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A, P	US 5,686,596 A (MUKHERJEE) 11 November 1997, see entire document.	1-8, 15-25
A, P	FAJAS et al. The Organization, Promoter Analysis, and Expression of the Human PPAR gamma Gene. The Journal of Biological Chemistry. 25 July 1997, Vol. 272, No. 30, pages 18799-18789, see entire document.	1-8, 15-25
Y, P	US 5,726,041 A (CHRESPI et al.) 10 March 1998, see entire document.	1-8, 15-25
Y	GEARING et al. Structure of the Mouse Peroxisome Proliferator Activated Receptor alpha Gene. Biochemical and Biophysical Research Communications. 28 February 1994, Vol. 199, No. 1, pages 255-263, see entire document.	1-8, 15-25



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents:	*T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
*A* document defining the general state of the art which is not considered to be of particular relevance	*X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
*B* earlier document published on or after the international filing date	*Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
*L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	*Z* document member of the same patent family
*O* document referring to an oral disclosure, use, exhibition or other means	
*P* document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

25 SEPTEMBER 1998

Date of mailing of the international search report

28 OCT 1998

Name and mailing address of the ISA/US  
Commissioner of Patents and Trademarks  
Box PCT  
Washington, D.C. 20231

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Telephone No. (703) 308-0196

**INTERNATIONAL SEARCH REPORT****International application No.**  
**PCT/US98/15411****C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT**

<b>Category*</b>	<b>Citation of document, with indication, where appropriate, of the relevant passages</b>	<b>Relevant to claim No.</b>
<b>Y</b>	<b>ZHU et al. Structural organization of mouse peroxisome proliferator-activated receptor gamma (mPPARgamma) gene: Alternative promoter use and different splicing yield two mPPR gamma isoforms. Proceedings of National Academy of Sciences, U.S.A. August 1995, Vol. 92, pages 7921-7925, see entire document.</b>	<b>1-8, 15-25</b>



# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US98/15411

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
  
2. ☒ Claims Nos.: 9-14  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:  
  
Please See Extra Sheet.
  
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
  
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.  
☐ No protest accompanied the payment of additional search fees.

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US98/15411

## A. CLASSIFICATION OF SUBJECT MATTER:

IPC (6):

C07H 21/02, 21/04; C12N 5/06, 5/08, 5/10; C12Q 1/02, 1/68; C12P 21/06

## B. FIELDS SEARCHED

Electronic data bases consulted (Name of data base and where practicable terms used):

APS, STN (CAPLUS), DIALOG (MEDLINE, BIOSIS, SCISEARCH)

TERMS: PPAR, peroxisome proliferator activated receptor?, genom? clon? untranslate? region? sequence? regulat? control? element? human?

## BOX I. OBSERVATIONS WHERE CLAIMS WERE FOUND UNSEARCHABLE

2. Where no meaningful search could be carried out, specifically:

The above claims are drawn to specific sequences or specific regions (subsequences) of particular genes. The CRF submitted in response to a telephone call to Applicant's representative did not comply with the sequence rules. Applicant's representative was FAXed a copy of the error report, but has not yet submitted a subsequent CRF.

**FOR THE PURPOSES OF INFORMATION ONLY**

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

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BY	Belarus	IS	Iceland	MW	Malawi	US	United States of America
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CN	China	KR	Republic of Korea	PT	Portugal		
CU	Cuba	KZ	Kazakstan	RO	Romania		
CZ	Czech Republic	LC	Saint Lucia	RU	Russian Federation		
DE	Germany	LI	Liechtenstein	SD	Sudan		
DK	Denmark	LK	Sri Lanka	SE	Sweden		
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1

## SEQUENCE LISTING

<110> Michael R. Briggs  
Regis S. Saladin  
Johan Auwerx  
Lluís Fajás

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(PPAR $\gamma$ ) GENE REGULATORY SEQUENCES AND USES THEREFOR

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&lt;212&gt; DNA

&lt;213&gt; LF-20

&lt;400&gt; 7

cattccattc acaagaacag atccagtgt

30

&lt;210&gt; 8

&lt;211&gt; 30

&lt;212&gt; DNA

&lt;213&gt; LF-21

&lt;400&gt; 8

ggctcttcat gaggcttatt gtagagctga

30

&lt;210&gt; 9

&lt;211&gt; 29

5

&lt;212&gt; DNA

&lt;213&gt; LF-22

&lt;400&gt; 9

gcaattgaat gtcgtgtctg tggagataa

29

&lt;210&gt; 10

&lt;211&gt; 29

&lt;212&gt; DNA

&lt;213&gt; LF-23

&lt;400&gt; 10

gtggatccga cagttaagat cacatctgt

29

&lt;210&gt; 11

&lt;211&gt; 30

&lt;212&gt; DNA

&lt;213&gt; LF-24

&lt;400&gt; 11

gtagaaataa atgtcagtac tgtcggtttc

30

&lt;210&gt; 12

&lt;211&gt; 29

&lt;212&gt; DNA

&lt;213&gt; LF-25

&lt;400&gt; 12

tcgatatcac tggagatctc cgccaacag

29

&lt;210&gt; 13

&lt;211&gt; 30



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6

&lt;212&gt; DNA

&lt;213&gt; LF-26

&lt;400&gt; 13

acataaaagtc cttcccgctg accaaagcaa

30

&lt;210&gt; 14

&lt;211&gt; 29

&lt;212&gt; DNA

&lt;213&gt; LF-27

&lt;400&gt; 14

ctctgctcct gcaggggggt gatgtgttt

29

&lt;210&gt; 15

&lt;211&gt; 29

&lt;212&gt; DNA

&lt;213&gt; LF-28

&lt;400&gt; 15

gaagttcaat gcactggaat tagatgaca

29

&lt;210&gt; 16

&lt;211&gt; 29

&lt;212&gt; DNA

&lt;213&gt; LF-29

&lt;400&gt; 16

gagctccagg ggttgtagca ggttgtctt

29

&lt;210&gt; 17

&lt;211&gt; 28

&lt;212&gt; DNA

<213> LF-33

<400> 17

gacgggctga ggagaagtca cactctga

28

<210> 18

<211> 28

<212> DNA

<213> LF-35

<400> 18

agcatggaat aggggtttgc tgtaattc

28

<210> 19

<211> 24

<212> DNA

<213> LF-36

<400> 19

tagtacaagt cctttagat ctcc

24

<210> 20

<211> 24

<212> DNA

<213> LF-44

<400> 20

gtcggcctcg aggacaccgg agag

24

<210> 21

<211> 24

<212> DNA

<213> LF-58

WO 99/05161

PCT/US98/15411

8

&lt;400&gt; 21

cactcatgtg acaagacctg ctcc

24

&lt;210&gt; 22

&lt;211&gt; 24

&lt;212&gt; DNA

&lt;213&gt; LF-59

&lt;400&gt; 22

gccgacacta aaccaccaat atac

24

&lt;210&gt; 23

&lt;211&gt; 24

&lt;212&gt; DNA

&lt;213&gt; LF-60

&lt;400&gt; 23

cgttaaaggc tgactctcgt ttga

24

&lt;210&gt; 24

&lt;211&gt; 26

&lt;212&gt; DNA

&lt;213&gt; AII J PPRE

&lt;400&gt; 24

gataccttcaa cctttaccct ggtaga

26

&lt;210&gt; 25

&lt;211&gt; 30

&lt;212&gt; DNA

&lt;213&gt; ACO PPRE

&lt;400&gt; 25

gatccccgaac gtgacctttg tcttggtccc

30

&lt;210&gt; 26

&lt;211&gt; 27

&lt;212&gt; DNA

&lt;213&gt; LPL PPRE

&lt;400&gt; 26

gatccgtctg cccctttcccc ctcttca

27

&lt;210&gt; 27

&lt;211&gt; 19

&lt;212&gt; DNA

<213>  $\gamma$  AS

&lt;400&gt; 27

gcattatgag catccccac

19

&lt;210&gt; 28

&lt;211&gt; 20

&lt;212&gt; DNA

<213>  $\gamma$ S

&lt;400&gt; 28

tctctccgta atggaagacc

20

&lt;210&gt; 29

&lt;211&gt; 19

&lt;212&gt; DNA

<213>  $\gamma$ 2S

10

&lt;400&gt; 29

gcgattcctt cactgatac

19

&lt;210&gt; 30

&lt;211&gt; 52

&lt;212&gt; DNA

&lt;213&gt; CDS

&lt;400&gt; 30

ttctagaatt cagcggccgc tttttttttt tttttttttt tttttttttt vn

52

&lt;210&gt; 31

&lt;211&gt; 201

&lt;212&gt; DNA

&lt;213&gt; PPARy1 proximal promoter

&lt;400&gt; 31

acccccaccc ccacccccag ccggcgcccc cgcccccccc cgcgccgggc ccggctcggc	60
ccgacccgga tccgcccgcg cgggcaggcg gggcccagcg cactcggagc ccgagcccga	120
gccgcagccg ccgcctgggg cgcttgggtc ggcctcgagg acaccggaga ggggcgccac	180
gccgcctggt ccgcagaaat g	201

&lt;210&gt; 32

&lt;211&gt; 177

&lt;212&gt; DNA

&lt;213&gt; PPARy2 proximal promoter

&lt;400&gt; 32

gtcctttctg tgttttattcc catctctccc aaatatttgg aaactgatgt cttgactcat	60
gggtgtattc acgattctgt tacttcaagt ctttttcttt taacggattg atcttttgct	120
agatagagac aaaatatcag tgtgaattac agcaaacca tattccatgc tgttatg	177

&lt;210&gt; 33

&lt;211&gt; 468

&lt;212&gt; DNA

<213> PPAR $\gamma$ 3 proximal promoter

&lt;400&gt; 33

taatcctttt	aaggtctagt	ttttcttaag	tctgtgcagt	aatagaggta	tcgtcattca	60
tgtgacataa	aagatggaaa	ggggcttcat	tcatgttagt	gatggaaata	ggaaagtagg	120
tgaagtgatt	ttaatagatg	tttcttttat	gaaataattt	ttaaagattg	tccagccctg	180
catgatttat	gatgaatcat	tttgtggtct	gttagttact	tttagagaat	agaaagcatt	240
gtaggctcag	ggaaagcaaa	cattcagaat	gaaatccaat	agagaaggta	aattttattg	300
ggcatgtaca	ttttggcagc	ctaggctgtg	tacatgtgta	cacattctga	acatgtgtgt	360
atattgaaaa	tcttgtctct	tttttattgt	taagatttga	aagaagccga	cactaaacca	420
ccaatataca	acaaggccat	tttgtcaaac	gagagtcagc	ctttaacg		468

&lt;210&gt; 34

&lt;211&gt; 1433

&lt;212&gt; DNA

<213> PPAR $\gamma$ 3 promoter, exon A2, and intron A2

&lt;400&gt; 34

gagaatacag	gcacatgcca	ccatgcccag	ctaatttttc	tgttttttgt	agagacagga	60
tttcgctgtg	gtgctcaggc	tggtctccaa	ctcctgggct	caagcaatcc	gcctgcctca	120
gccttccaaa	gtgaaaagg	tttctctcat	ttttcaaata	gaagtactaa	acaatgccag	180
agaaataaat	aaacaggcaa	aatacgttgg	ctatagttta	tattatttcc	tgctacagtt	240
aacaaaatgg	gaagacattt	tatcttcatg	gtctactaca	tttatgccat	gtgttaagta	300
ataaaatagc	ttttgtaaat	tataaattaa	aaggtagaca	tttaaaagag	aaaatactgt	360
agagttttca	tgtaggtaag	actgtgtaga	atgtcgggtc	tcgatgttgg	cgctattcaa	420
gccctgatga	taaggctttt	ggcattagat	gctgttttgt	cttcatggaa	aatacagcta	480
ttctaggatc	cttgagcctt	tcataagaga	taaggttgtg	aatcctaaga	ccctaggacc	540
atttacttag	atgatctgct	ctctggttcg	tcctctgaaa	agtctgcttc	gtgaggggtg	600
tgctgcattt	gccttgccct	agtgggtgtg	cacacaactg	tactgtcacc	ttaggcttaa	660
taaccatgtg	tcatctagaa	tgaagttata	ttttaaaaag	gacgtttttt	gccatgtata	720
aattttcaaa	cattaacttt	cagggttatt	aatcctttta	aggtctagtt	tttcttaagt	780
ctgtgcagta	atagagggtat	cgtcattcat	gtgacataaa	agatggaaaag	gggcttcatt	840
catgttagtg	atggaaaatag	gaaagtaggt	gaagtgattt	taatagatgt	ttctttttatg	900
aaataatttt	taaaagattg	tccagccctg	catgatttat	gatgaatcat	tttgtggtct	960
gttagttact	tttagagaat	agaaagcatt	gtaggctcag	ggaaagcaaa	cattcagaat	1020
gaaatccaat	agagaaggta	aattttattg	ggcatgtaca	ttttggcagc	ctaggctgtg	1080
tacatgtgta	cacattctga	acatgtgtgt	atattgaaaa	tcttgtctct	tttttattgt	1140
taagatttga	aagaagccga	cactaaacca	ccaatataca	acaaggccat	tttctcaaac	1200
gagagtcagc	ctttaacggg	aagtaaaatc	agaattttata	ctgcatttgt	attgaaaagt	1260
atccctttta	aagaatatgt	aaattataca	ttgttatttt	attgtaaaat	ttcctagaga	1320
gtgatttttg	actattataa	tactttctgc	tatataattt	tccagtcagt	tggactatgc	1380
agtgtaacat	atttgtctaa	cacaaaacaa	aggtaagata	ggaaaatgac	ctagaagttg	1440
agaaataact	caaatcctta	aaa				1433

12

&lt;210&gt; 35

&lt;211&gt; 695

&lt;212&gt; DNA

&lt;213&gt; Intron B, exon 1, and intron 1

&lt;400&gt; 35

```

ctgggataac aggtgtgagc cactgtgcct ggccctgtata ctataagttt aaaatttttg 60
tctattatac tcaataaagc tggacaaaat tttaaataaa taacagcagt cattaacaga 120
ctcaattgat gacctaatgt agaagttaat gagagcaggc ctggttgcaa aaaggcattt 180
atatggatac actgtatgta tctgcactgt ttcaggatcc tctattatga tacctgggta 240
aagggtgact tcctttctat cataaaacag cctagacagc actaagaagg tggttatggt 300
cttttctgtt gttgtgagcg cccagatgag attactttgc caaagactct ttctatttct 360
ctttctgaaa ctctgtgaga ttgctgtgtt ctctaggact taacttcaca gctagtctat 420
ttttcctttc agaaatgacc atggttgaca cagagatgcc attctggccc accaactttg 480
ggatcagctc cgtggatctc tccgtaatgg aagaccactc ccactccttt gatatcaagc 540
ccttcactac tgttgacttc tccagcattt ctactccaca ttacgaagac attccattca 600
caagaacaga tccagtgggt gcagattaca agtatgacct gaaacttcaa gagtaccaa 660
gtatgatgtt tgttttcact tttcagacta ctagg 695

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&lt;210&gt; 36

&lt;211&gt; 313

&lt;212&gt; DNA

&lt;213&gt; Intron 1, exon 2, and intron 2

&lt;400&gt; 36

```

ctgttttcat gggataatta tcctctcaca tgtctccata cacaggtgca atcaaagtgg 60
agcctgcac tccacottat tattctgaga agactcagct ctacaataag cctcatgaag 120
agccttcaa ctcctcatg gcaattgaat gtcgtgtctg tggagataaa gcttctggat 180
ttcactatgg agttcatgct tgtgaaggat gcaaggtaat taacaaataa gtcttcaaag 240
aaattgttga aactttatta tttcatttca gcagaacccc ttttttaggt gatacaatat 300
atgaattttt ttt 313

```

&lt;210&gt; 37

&lt;211&gt; 473

&lt;212&gt; DNA

&lt;213&gt; Intron 2, exon 3, and intron 3

&lt;400&gt; 37

```

gatacctttc gctgtaggtt cgtgcttcca tgtgtcataa agacttaaaa tttgcttctt 60

```

13

```

ttttatccct ttgcagggtt tcttccggag aacaatcaga ttgaagctta tctatgacag 120
atgtgatctt aactgtcggg tccacaaaaa aagtagaaat aaatgtcagt actgtcgggt 180
tcagaaatgc cttgcagtgg ggatgtctca taatggtaag taaacagtca tcaccatata 240
ctttattatt ctcattatag ctgccagacc agtggacact aaagccattg ccaaaaaatgt 300
gtacagtttt tccaccaaatt gccagaattt agaattattgc atggcgataa aacattttctc 360
ttttagggtca gtgttttttaa agttttatta tagaaccttt ctctctgtgg ttgggcatct 420
gccatgagga gaaaagagac ttgaaaaatc tgggggatta tgggaaaaaac ctt 473

```

&lt;210&gt; 38

&lt;211&gt; 706

&lt;212&gt; DNA

&lt;213&gt; Intron 3, exon 4, and intron 4

&lt;400&gt; 38

```

acaactttga attctgcaca gtttcgtatt ttaattcgtg aaacgtgttg atccttctaa 60
gtgcctgacc ttaggtcaag tgctggggat acaaagaagg tgacctttga attgggtctt 120
gagggatgag taggagttgg ttctcaatta ttacagttt aagtcgacat acttccctcc 180
ctttgctaaa ctgaattctt ttcactttct cagcaggagt atgcattaac ttttaaaaat 240
gaaagttaac ggtttaattt ttactgatgg tctgtgctac tttgtgaaa taaaaacatg 300
agcaaagtgg tagacagaaa ccaggactca agagcagtgg aggaggaggg cttctactgt 360
gtgggaacga gggctgggag agcacagtgt gtgttcagag cagtagtaat ccaatgattc 420
atcctgtcat tctcttctct ctatagccat caggtttggg cggtatgccac aggccgagaa 480
ggagaagctg ttggcggaga tctccagtga tatcgaccag ctgaatccag agtccgctga 540
cctccgtgcc ctggcaaaac atttgtatga ctcatacata aagtccttcc cgctgaccaa 600
agcaaaggcg agggcgatct tgacaggaaa gacaacagac aaatcagtta gttctcttct 660
gctgtcttca ttgggggagg cgggaagttg ttttgggatt tttgtt 706

```

&lt;210&gt; 39

&lt;211&gt; 732

&lt;212&gt; DNA

&lt;213&gt; Intron 4, exon 5, and intron 5

&lt;400&gt; 39

```

gggaaagaag accaaaattg gtgaaatatg tttgggccca gaagataatt aagatgaata 60
aaagaacttg agagtatttt ctcattatta agcatcttca gctttaaaga ttttagttag 120
caaagcaagt ttacataaac agttttctga acctgggagtg gcattcactg tgagttagaa 180
atctccaagt catcccacgt tttccctgtt ttatttgcag ccattcgtta tctatgacat 240
gaattcctta atgatgggag aagataaaat caagttcaaa cacatcaccc ccctgcagga 300
gcagagcaaa gaggtggcca tccgcattct tcagggtctgc cagtttcgct ccgtggaggc 360
tgtgcaggag atcacagagt atgccaaaag cattcctggt ttgtaaaatc ttgacttgaa 420
cgaccaagta actctcctca aatatggagt ccacgagatc atttacacaa tgctggcctc 480
cttgatgaat aaagatgggg ttctcatatc cgagggccaa ggcttcatga caaggaggtt 540
tctaaagagc ctgcgaaagc cttttggtga ctttatggag cccaagtttg agtttgcgtg 600
gaagttcaat gactggaat tagatgacag cgacttggca atatttattg ctgtcattat 660
tctcagtggg ggttaagattt gtcttttgat cttctatgaa agagggtggg atgatggtg 720
ggtggccaaa ag 732

```



14

&lt;210&gt; 40

&lt;211&gt; 592

&lt;212&gt; DNA

&lt;213&gt; Intron 5, exon 6, and 3' UTR

&lt;400&gt; 40

```

tccccaccta tttaagatac aaagcaaaac aaaccaaaaa tacagatgag ttgcttggtg 60
gagntgcnta ggccctccaag gcgggggcca gaggattttt tgactgaacc ccctgttggtg 120
ttttccatat gtgcttcccc agaccgcca ggtttgctga atgtgaagcc cattgaagac 180
attcaagaca acctgctaca agccctggag ctccagctga agctgaacca ccctgagtcc 240
tcacagctgt ttgccaagct gctccagaaa atgacagacc tcagacagat tgtcacggaa 300
cacgtgcagc tactgcaggt gatcaagaag acggagacag acatgagtct tcacccgctc 360
ctgcaggaga tctacaagga cttgtactag cagagagtcc tgagccactg ccaacatttc 420
ccttcttcca gttgcactat tctgaggga aatctgacca taagaaattt actgtgaaaa 480
agcgttttaa aaagaaaagg gtttagaata tgatctattt tatgcatatt gtttataaag 540
acacatttac aatttacttt taatattaaa aattaccata ttatgaaatt gc 592

```

&lt;210&gt; 41

&lt;211&gt; 13

&lt;212&gt; DNA

<213> PPAR $\gamma$ 3-E-box

&lt;400&gt; 41

attcatgtga cat

13

&lt;210&gt; 42

&lt;211&gt; 13

&lt;212&gt; DNA

<213> PPAR $\gamma$ 3-E-box

&lt;400&gt; 42

attcatgcat cat

13

&lt;210&gt; 43

&lt;211&gt; 13

15

&lt;212&gt; DNA

&lt;213&gt; A1 (97) Donor

&lt;400&gt; 43

cgcaggtcag agt

13

&lt;210&gt; 44

&lt;211&gt; 13

&lt;212&gt; DNA

&lt;213&gt; A1 (97) Acceptor

&lt;400&gt; 44

ttgttaagat ttg

13

&lt;210&gt; 45

&lt;211&gt; 13

&lt;212&gt; DNA

&lt;213&gt; A2 (74) Donor

&lt;400&gt; 45

taacggtaag taa

13

&lt;210&gt; 46

&lt;211&gt; 13

&lt;212&gt; DNA

&lt;213&gt; A2 (74) Acceptor

&lt;400&gt; 46

cctttcagaa atg

13

&lt;210&gt; 47

&lt;211&gt; 12

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16

&lt;212&gt; DNA

&lt;213&gt; B (211) Donor

&lt;400&gt; 47

caaggtaaag tt

12

&lt;210&gt; 48

&lt;211&gt; 13

&lt;212&gt; DNA

&lt;213&gt; B (211) Acceptor

&lt;400&gt; 48

ccttttcagaa atg

13

&lt;210&gt; 49

&lt;211&gt; 12

&lt;212&gt; DNA

&lt;213&gt; 1 (213) Donor

&lt;400&gt; 49

caaagtatga tg

12

&lt;210&gt; 50

&lt;211&gt; 13

&lt;212&gt; DNA

&lt;213&gt; 1 (231) Acceptor

&lt;400&gt; 50

atacacaggt gca

13

&lt;210&gt; 51

&lt;211&gt; 12

WO 99/05161

PCT/US98/15411

17

&lt;212&gt; DNA

&lt;213&gt; 2 (170) Donor

&lt;400&gt; 51

caaggtaatt aa

12

&lt;210&gt; 52

&lt;211&gt; 12

&lt;212&gt; DNA

&lt;213&gt; 2 (170) Acceptor

&lt;400&gt; 52

ctttgcaggg tt

12

&lt;210&gt; 53

&lt;211&gt; 12

&lt;212&gt; DNA

&lt;213&gt; 3 (139) Donor

&lt;400&gt; 53

aatggtaagt aa

12

&lt;210&gt; 54

&lt;211&gt; 13

&lt;212&gt; DNA

&lt;213&gt; 3 (139) Acceptor

&lt;400&gt; 54

ctctatagcc atc

13

&lt;210&gt; 55

&lt;211&gt; 12

WO 99/05161

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18

&lt;212&gt; DNA

&lt;213&gt; 4 (203) Donor

&lt;400&gt; 55

atcagttagt tc

12

&lt;210&gt; 56

&lt;211&gt; 12

&lt;212&gt; DNA

&lt;213&gt; 4 (203) Acceptor

&lt;400&gt; 56

atttgcagcc at

12

&lt;210&gt; 57

&lt;211&gt; 12

&lt;212&gt; DNA

&lt;213&gt; 5 (451) Donor

&lt;400&gt; 57

ggaggtaga tt

12

&lt;210&gt; 58

&lt;211&gt; 13

&lt;212&gt; DNA

&lt;213&gt; 5 (451) Acceptor

&lt;400&gt; 58

ttccccagac cgc

13

&lt;210&gt; 59

&lt;211&gt; 12

19

&lt;212&gt; DNA

&lt;213&gt; 6 (248) Donor

&lt;400&gt; 59

tactagcaga ga

12

&lt;210&gt; 60

&lt;211&gt; 44

&lt;212&gt; DNA

&lt;213&gt; Adaptor

&lt;400&gt; 60

ctaatacgac tcactatagg gctcgagcgg ccgcccgggc aggt